Original Article*

Mortality Rates Due to Diabetes in a Selected Urban South Indian Population - The Chennai Urban Population Study [CUPS - 16]

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Abstract

Objective : The aim of this study was to determine the mortality rate in diabetic and non-diabetic subjects in urban south India.

Methods : The Chennai Urban Population Study is an ongoing epidemiological study in Chennai [formerly Madras, in south India]. All individuals ≥ 20 years of age living in two residential colonies in Chennai were invited to participate in the study. Of the total 1399 eligible subjects, 1262 individuals responded [90.2%] at baseline, and of these, 1140 individuals [90.3%] could be followed annually from 1997 to 2003-04. Mortality rates and causes of death were the main outcome measures.

Results : The median follow up period was six years. The overall mortality rate was higher in diabetic compared to non-diabetic subjects [18.9 vs.5.3 per 1000 person-years, p=0.004]. Mortality due to cardiovascular [diabetic subjects, 52.9%; non-diabetic subjects, 24.2%,p=0.042] and renal causes[diabetic subjects, 23.5%; non-diabetic subjects, 6.1%,p=0.072] was higher among diabetic subjects whereas mortality due to gastrointestinal [12.1%], respiratory [9.1%], lifestyle related [6.1%] and unnatural causes [18.2%] were observed only among non-diabetic subjects. Hazards ratio [HR] for all cause mortality for diabetes was 3.6, [95% Confidence Interval [CI]: 2.02-6.53, p<0.001] and this remained significant even after adjusting for age [HR:1.9, 95% CI:1.04-3.45, p=0.038]. Light grade physical activity was associated with higher mortality rate [p=0.008], but the significance disappeared when adjusted for age. Smoking was also associated with increased mortality.

Conclusions : In urban India, mortality rates are two fold higher in people with diabetes compared to non-diabetic subjects. Cardiovascular and renal diseases are the commonest causes of death among diabetic subjects. ©

Migrant Asian Indians have higher prevalence rates of diabetes, premature coronary artery disease and cardiovascular disease [CVD] mortality compared to the host populations of these countries.[1-3] Asian Indians with diabetes also have higher mortality rates compared to diabetic subjects of other ethnic groups.[4] According to recent reports, the prevalence rates of diabetes and coronary artery disease in urban India are now similar to migrant Asian Indians.[5,6] Indeed, India already has the largest number of people with diabetes in the world and it is also predicted to lead in coronary artery disease deaths in the next fifteen years.[7] A recent report published by the Indian Council of Medical Research (ICMR) in 2004, reported that in India, diabetes accounts for 1.09 lakh deaths/ year.[8] However, there are very few population-based studies on mortality rates in India and virtually none comparing diabetic and non-diabetic subjects. In this paper, we report on mortality data among diabetic and non-diabetic subjects in a population-based study in urban south India.

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Subjects And Methods

Baseline studies

The Chennai Urban Population Study [CUPS], an ongoing epidemiological study in two residential colonies in Chennai [formerly Madras, the largest city in southern India] was started in 1996 and the baseline study was completed in 1997. The methodological details and several reports from CUPS have been published.[9,10] Briefly, all individuals ≥ 20 years of age were invited to participate in a screening programme for diabetes. The overall response rate was 90.2%.

Anthropometric measures [weight, height, waist and hip] and blood pressure were measured using standard methods. A resting 12-lead electrocardiogram [ECG] was carried out on 1175 subjects [response rate - 84%].

A fasting blood sample was taken for estimation of glucose and lipids following which an oral glucose load [75 gm] was administered to all individuals [excluding known diabetic subjects]. All biochemical assays were done using a Corning Express Plus Auto Analyser [Corning, Medfield, MA, USA] using kits supplied by Boehringer Mannheim [Mannheim, Germany].

Individuals were categorized based on a validated physical activity [PA] questionnaire as having light, moderate and heavy activity.[10]

Follow up data on mortality

From 1997, annual visits were made to every household and details of all deaths were recorded. The last visit was conducted between October 2003 and August 2004.

Causes of death: Unfortunately autopsies are usually not performed in India except in some medico-legal cases. We had to therefore make use of all available sources of information to determine possible cause of death. These included interview of family members and wherever available, scrutiny of hospital records or the deceased's medical files, police records [where relevant] and death certificates issued by the Corporation of Chennai, the official body for registration of all deaths in Chennai.

Causes of death were coded as: cardiovascular or CVD [heart failure, myocardial infarction or stroke], renal, gastrointestinal [gastrointestinal bleeding, cirrhosis or hepatitis], respiratory [tuberculosis or chronic obstructive pulmonary disease], cancer, lifestyle-related [eg alcoholism], unnatural causes [suicides, accident], others [deaths due to infection or aging] and the rest as unknown causes.

Definitions

Type 2 diabetes was diagnosed based on WHO consulting group criteria. Hypertension was diagnosed using the JNC-VI criteria. Coronary artery disease [CAD] was diagnosed based on a documented past history of myocardial infarction or drug treatment for coronary artery disease and / or Minnesota codes 1-1-1 to 1-1-7, [Q wave changes] 4-1 to 4-2 [ST segment depression] or 5-1 to 5-3 [T wave abnormalities].[6]

Individuals were classified as non-smokers and current smokers [habitual smokers regardless of quantity smoked]. Alcohol intake was categorized as none, social [occasional drinking] and regular [everyday intake regardless of the quantity consumed].

Statistical Analysis

Mortality rates were calculated as number of deaths per 1000 person-years of follow-up. Statistical analysis was carried out using the SPSS PC Windows version 10.0 [Chicago, IL]. Students "t" test was used to compare means and Chi Square or Fischer's exact test to compare proportions. Cox regression analysis was used to determine the effect of various risk factors on mortality. Survival curves were plotted by life-table analysis and those of subjects with and without diabetes were compared using Wilcoxon [Gehan] test.

Results

Of the 1262 individuals who initially participated in CUPS, 90 shifted their residence to another colony within Chennai, 79 moved out of the state of Tamil Nadu and 23 left the country. We were able to obtain follow-up data on all those who continued to reside in the same colonies and 70 of the 90 who shifted their residence to another colony within Chennai i.e. on a total of 1140 individuals [response rate: 1140 / 1262 – 90.3%] [Fig. 1]. The response rates among diabetic and non-diabetic subjects were 94.1% and 89.8% respectively.

There were no significant differences in the baseline characteristics of the responders [n = 1140] and non-responders [n = 122] with respect to age: 43 ± 16 vs. 42 ± 16 years; gender: males: 44.5% vs. 41.0%; prevalence of diabetes: 14.5% vs. 12.3% or prevalence of coronary artery disease: 11.1% vs. 9.5%. However, the prevalence of hypertension was higher among the responders compared to non-responders [23.1% vs. 13.1%, p=0.012].

During the median follow up period of six-years, fifty deaths [50 / 1140, 4.4%] were observed yielding an overall all-cause mortality rate of 7.0 per 1,000 person-years.

The percentage of deaths was significantly higher among diabetic subjects [17 / 143, 11.9%] compared to non-diabetic subjects [33 / 997, 3.3%, p <0.001] [Fig. 1]. This translates to an all-cause mortality of 18.9 per 1000 person years among diabetic subjects compared to 5.3 per 1000 person-years among non-diabetic subjects [Table 1].

Mortality due to CVD [52.9% vs. 24.2%,p=0.042] and renal causes [23.5% vs. 6.1%,p=0.072] were higher

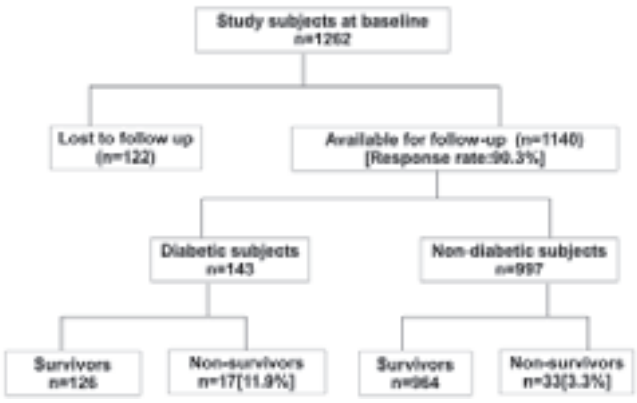

Fig. 1 : Flow-chart of the study protocol.

Table 1 : Causes of death in the population

Cause of death	Total deaths (n = 50)	Non-diabetic subjects (n = 33)	Diabetic subjects (n = 17)
Cardiovascular n (%)	17 (34)	8 (24.2)	9 (52.9)
Renal n (%)	6 (12)	2 (6.1)	4 (23.5)
Gastrointestinal mortality n (%)	4 (8)	4 (12.1)	0
Respiratory n (%)	3 (6)	3 (9.1)	0
Cancer n (%)	3 (6)	3 (9.1)	0
Unnatural causes n (%)	6 (12)	6 (18.2)	0
Lifestyle-related n (%)	2 (4)	2 (6.1)	0
Others			
Age-related n (%)	2 (4)	1 (3.0)	1 (5.9)
Infections n (%)	2 (4)	1 (3.0)	1 (5.9)
Unknown n (%)	5 (10)	3 (9.1)	2 (11.8)
Mortality rate per 1000 person-years*	7.0	5.3	18.9 #

Numbers in parenthesis are percentages; * Mortality rates were calculated as the number of subjects died by person-years of follow-up and are expressed as per 1000 person-years. # p=0.004 compared to non-diabetic subjects

Table 2 : Baseline demographic, clinical and biochemical characteristics by diabetes status and all-cause mortality

Parameters	Non-diabetic subjects		Diabetic subjects	
	Survivors (n = 964)	Non-survivors (n = 33)	Survivors (n = 126)	Non-survivors (n = 17)
Age (yrs.)	41 ± 14	54 ± 16 ***	54 ± 11	66 ± 12 ***
Male n (%)	420 (43.6%)	16 (48.5%)	64 (50.8%)	7 (41.2%)
Systolic blood pressure (mm Hg)	119 ± 22	123 ± 20	131 ± 14	139 ± 17 *
Diastolic blood pressure (mm Hg)	77 ± 14	79 ± 12	84 ± 10	87 ± 11
Body mass index (kg/m^2)	22.3 ± 4.4	21.0 ± 5.1	25.3 ± 4.0	23.1 ± 4.7 *
Waist circumference (cm)	76 ± 13	65 ± 19 **	87 ± 11	81 ± 11 *
Fasting plasma glucose (mg/dl)	76 ± 17	77 ± 15	153 ± 79	169 ± 131
Serum cholesterol (mg/dl)	167 ± 44	165 ± 40	199 ± 53	186 ± 66
Serum triglycerides (mg/dl)	111 ± 70	95 ± 32 *	172 ± 98	123 ± 55 *
Hypertension n (%)	185 (19.2%)	9 (27.3%)	57 (45.2%)	12 (70.6%) *
Coronary artery disease n (%)	86 (9.5%)	5 (16.7%)	21 (17.5%)	7 (43.8%)
Smoking n (%)	133 (13.8%)	10 (30.3%) **	9 (7.1%)	1 (5.9%)
Alcohol n (%)	237 (24.6%)	13 (39.4%)	29 (23.0%)	3 (17.6%)

* p < 0.05, ** p < 0.01, *** p < 0.001 compared to survivors

among diabetic, compared to non-diabetic subjects. Deaths due to gastrointestinal [12.1%], respiratory [9.1%], lifestyle related [6.1%] and unnatural causes [18.2%] were observed only among non-diabetic subjects [Table 1].

The mean age of death among diabetic subjects was 66 years compared to 54 years among non-diabetic subjects [Table 2]. The mean age of subjects who died of CVD causes was 65 ±11 years and 24% were less than 50 years old.

Among non-diabetic subjects who died, the proportion of smokers was significantly higher [p<0.001]. Waist circumference [p=0.004] and triglyceride levels [p<0.05] were lower among the non-survivors compared to the survivors. Among diabetic non-survivors, proportion of hypertensives were significantly higher [p<0.05] and they also had significantly higher systolic blood pressure values [p=0.035]. However body mass index [p=0.036], waist circumference [p=0.026] and triglycerides were lower compared to the survivors. None of the other parameters showed any significant difference.

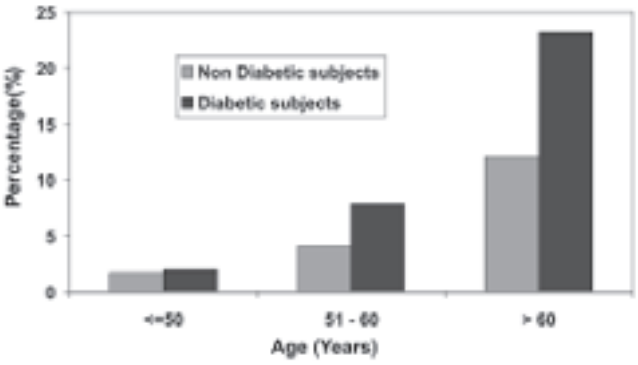

Fig. 2 : Age wise distribution of deceased in both diabetic and non-diabetic subjects.

Mortality increased with increase in age intervals [age ≤ 50 years: 1.8%, 51-60 years: 5.0%, >60 years: 15.6%, trend chi-square: 62.8, p<0.001]. When diabetic and non-diabetic subjects were compared, at any given age interval, diabetic subjects had increased death rates compared to the non-diabetic subjects but the differences did not reach statistical significance [diabetic vs non-

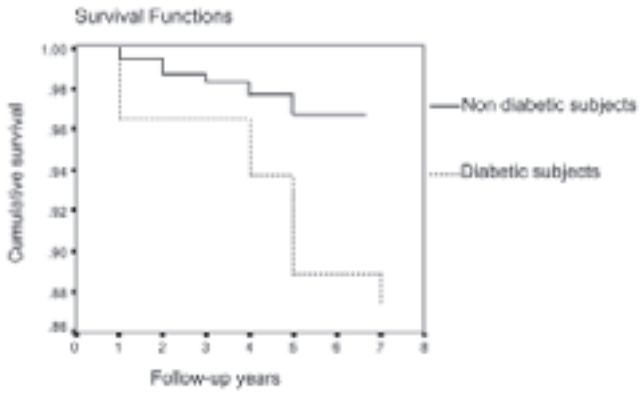

Fig. 3 : Survival curves for diabetic and non-diabetic subjects

diabetic, age ≤ 50 years : 2.0% vs. 1.7%, p=0.874, 51-60 years: 7.9% vs. 4.1%,p=0.342 >60 years: 23.2% vs. 12.1%,p=0.057] [Fig. 2].

Subjects who performed light grade activity had higher death rates compared to subjects with heavy grade activity [6.5% vs. 2.7%, p=0.008]. The hazards ratio [HR] for mortality among those with light grade activity was 2.39 [95% confidence intervals [CI]: 1.05-5.40, p=0.037] compared to heavy grade activity. However, the significance disappeared when adjusted for age [HR: 1.41, 95% CI: 0. 61-3.27, p=0.418].

The number of pack-years of smoking was significantly higher among the non-survivors [33.3 ±14.5] compared to survivors [14.8 ± 12.8, p<0.001]. All-cause mortality among smokers was 7.2% compared to 4.0% among non-smokers. The association of smoking with all-cause mortality remained significant even after age adjustment [HR: 2.84, 95% CI: 1.44 – 5.62, p=0.003].

The survival curves were significantly different in diabetic, compared to non-diabetic, subjects [Wilcoxon [Gehan] test: p<0.001] [Fig. 3].

Hazard ratio for all-cause mortality was higher for subjects with diabetes [HR: 3.6, 95% CI: 2.02-6.53, p<0.001] compared to non-diabetic subjects and this remained significant even after adjusting for age [HR: 1.9, 95% CI: 1.04-3.45, p=0.038]. The HR for diabetes for mortality due to CVD was 7.8 [95% CI: 3.0 –20.2, p<0.001, age adjusted: HR: 3.5, 95% CI: 1.3 – 9.1, p=0.012]. Diabetic subjects also had very high risk for renal mortality [unadjusted: HR: 14.3, 95% CI: 2.6 – 77.9, p<0.001. adjusted for age: HR: 10.7, 95% CI: 1.7 – 67.4, p=0.012].

Discussion

This is the first population-based study of mortality rates in diabetic and non-diabetic subjects from India and presents three major findings: first, mortality rates in diabetic subjects are twice as high as in non-diabetic subjects; second, cardiovascular and renal disease contributed to majority of deaths among diabetic subjects while lifestyle related, gastrointestinal and unnatural deaths were more common among non-diabetic subjects contributing to the lower age of death in the latter; finally, physical activity and smoking showed an association with all-cause mortality, but for the former, the significance disappeared when adjusted for age.

Earlier studies from India on mortality do not provide information on death rates in the general population.[11,12] In this study, we report that the overall mortality rate in the study population is 7.0 per 1000 person-years. The mean age at death was 58 years, and 24% of CVD mortality was seen among subjects less than 50 years of age confirming earlier reports of premature deaths due to CVD in Indians.[2,3] The lower age at death of non-diabetic subjects is perhaps fortuitous, probably due to the small numbers and also due to gastrointestinal, life-style related and unnatural causes. This scenario is likely to change with rapidly increasing prevalence of diabetes and control of communicable diseases in India.

Indeed, subjects with diabetes had two-fold higher risk for mortality compared to non-diabetic subjects, even after age adjustment and this corroborates earlier studies.[13-16] Survival rates were markedly lower among diabetic subjects and this was mostly due to CVD. The causes for increased cardiovascular deaths among diabetic subjects are multiple and include elevated glucose and blood pressure, dyslipidemia and inflammation. Multiple interventions are therefore needed to reduce cardiovascular risk in diabetic subjects.[17]

The second commonest cause of death in diabetic subjects was renal disease accounting for 23.5% of the deaths, which is similar to figures reported in other studies.[18] However, in contrast to earlier studies from India,[11,12,19] mortality due to infections was found to be less common. This might be due to the fact that earlier studies were hospital-based and referral bias could explain excess of deaths due to infections or may be due to misclassification bias.

In the Aerobics Center Longitudinal Study (ACLS) conducted among middle-aged men with type 2 diabetes, physical inactivity was an independent predictor of all-cause mortality.[20] The National Health Interview Survey (NHIS), which examined the relationship of walking and other physical activities to all cause mortality among US adults with diabetes reported that higher levels of physical activity were associated with a lower incidence of all-cause mortality.[21] Our finding demonstrates that physical inactivity was associated with all-cause mortality. However, age appears to be an effect modifier as it abolished the relation of physical inactivity with mortality. Surprisingly, the non-survivors had lower body mass index. This may reflect inadequate control of diabetes, resulting in weight loss. The lower triglyceride levels in the non-survivors can be explained by the use of lipid lowering drugs, as 16.7% of non-diabetic non-survivors and 43.8% among diabetic non-survivors had coronary

artery disease at baseline and hence were on treatment with lipid lowering drugs. Smoking was associated with all-cause mortality and this is similar to results in other populations.[22]

There are several limitations to this study. These include availability of soft evidence of cause of death due to improper filling of death certificates and inaccuracy of verbal accounts given by relatives of the deceased. Indeed, the cause of death was unknown in some cases due to non-availability of medical records. Moreover the cause of death recorded in death certificates may be unreliable as diabetes is rarely recorded as a cause of death.[23] Finally, the number of deaths is quite small as the original cohort itself consisted of only 1262 subjects. However, main strength of the study is that the data collected is from the community. The other strengths are that the response rate is very good, the data collected has helped to reasonably identify the cause of death in the population and this is the first paper from India to report on mortality due to diabetes. The results of the study can probably be extrapolated to most of urban India, as the prevalence rates of diabetes and CVD are fairly similar across most cities in India.[20] However in rural India, the prevalence of both diabetes and CVD is less than half of that in urban areas and hence mortality data is also likely to be quite different from that seen in urban areas.

In conclusion, this study highlights that diabetic subjects had higher mortality rates compared to non-diabetic subjects. Cardiac disease and renal diseases were the commonest cause for mortality in diabetic subjects. Smoking and physical inactivity are associated with all cause mortality.

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